

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently Amended) A method of ~~ameliorating a symptom of at least one-~~
~~degenerative disorder of muscle~~ for increasing muscle mass in an individual with a
disease or disorder in which an increase in muscle mass is desirable associated with-
GDF-8, comprising:

- (1) administering an effective amount of a pharmaceutical composition to a mammal, wherein the composition comprises an Activin Receptor Type IIB (ActRIIB) ~~ActRIIB~~ fusion polypeptide comprising (a) an amino acid sequence that is at least 95% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to growth and differentiation factor-8 (GDF-8) ~~GDF-8~~ and inhibiting a GDF-8 activity, wherein the GDF-8 activity is chosen from negative regulation of skeletal muscle mass, modulation of muscle-specific enzymes, stimulation of myoblast proliferation, and modulation of preadipocyte differentiation to adipocytes, and (b) an Fc portion of an antibody; and
 - (2) allowing the composition to inhibit GDF-8 activity, thereby ~~ameliorating a symptom of the degenerative disorder~~ increasing muscle mass in the individual.
2. (Original) The method of claim 1, wherein the mammal is human.
3. (Currently Amended) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of ~~ameliorating a symptom of a~~

~~disorder~~ disease or disorder is chosen from muscle disorder and neuromuscular disorder.

4. (Currently Amended) The method of ~~claim 4~~ claim 3, wherein the pharmaceutical composition is administered to a mammal in need of ameliorating a symptom of muscle disorder is a disorder chosen from at least one of muscular dystrophy, Duchenne's muscular dystrophy, muscle atrophy, and muscle wasting syndrome.

5. (Currently Amended) The method of ~~claim 4~~ claim 3, wherein the pharmaceutical composition is administered to a mammal in need of ameliorating a symptom of muscle disorder is Duchenne's muscular dystrophy.

6-9. (Canceled)

10. (Original) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need for repair of damaged muscle.

11. (Previously presented) The method of claim 10, wherein the damaged muscle is myocardiac muscle or diaphragm.

12. (Previously presented) The method of claim 1, wherein the ActRIIB fusion polypeptide is administered at an effective amount chosen from 1 µg/kg to 20 mg/kg, 1 µg/kg to 10 mg/kg, 1 µg/kg to 1 mg/kg, 10 µg/kg to 1 mg/kg, 10 µg/kg to 100 µg/kg, 100 µg to 1 mg/kg, and 500 µg/kg to 1 mg/kg.

13. (Original) The method of claim 1, wherein the first amino acid sequence of said ActRIIB fusion polypeptide comprises amino acids 23 to 138 of SEQ ID NO:3.

14. (Original) The method of claim 1, wherein the first amino acid sequence of said ActRIIB fusion polypeptide comprises amino acids 19 to 144 of SEQ ID NO:1.

15. (Original) The method of claim 1, wherein the second amino acid sequence of said ActRIIB fusion polypeptide comprises a sequence chosen from (a) the Fc fragment of IgG, (b) the Fc fragment of IgG1, (c) the Fc fragment of IgG4, and (d) amino acids 148 to 378 of SEQ ID NO:3.

16. (Original) The method of claim 1, wherein the sequence of the ActRIIB fusion polypeptide is set out in SEQ ID NO:3.

17. (Original) The method of claim 1, wherein circulatory half-life of the ActRIIB fusion polypeptide exceeds 5 days.

18-22. (Canceled)

23. (Currently Amended) The method of claim 1, wherein the fusion protein is encoded by a nucleic acid that hybridizes to the complement of SEQ ID NO:4 under stringent hybridization conditions (hybridization at about 65°C to 70°C in 4X SSC, or hybridization in 4X SSC plus 50% formamide at about 42-50°C; washing at about 65°C to 70°C in 1X SSC).

24. (Canceled)

25. (Withdrawn-Previously Presented) A method of inhibiting GDF-8 activity, comprising:

(1) contacting GDF-8 with a composition, wherein the composition comprises an ActRIIB fusion polypeptide comprising (a) an amino acid sequence that is at least 95% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to GDF-8, and (b) an Fc portion of an antibody; and

(2) allowing the composition to inhibit GDF-8 activity.

26. (Withdrawn-Previously Presented) A method of increasing muscle strength, said method comprising:

(1) administering an effective amount of a pharmaceutical composition to a mammal, wherein the composition comprises an ActRIIB fusion polypeptide comprising (a) an amino acid sequence that is at least 95% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to GDF-8, and (b) an Fc portion of an antibody; and

(2) allowing the composition to inhibit GDF-8 activity, thereby increasing muscle strength.

27-28. (Canceled)

29. (Previously Presented) The method of claim 1, wherein the amino acid sequence is at least 97% identical to amino acids 23 to 138 of SEQ ID NO:3.

30. (Previously Presented) The method of claim 1, wherein the amino acid sequence is at least 98% identical to amino acids 23 to 138 of SEQ ID NO:3.

31. (Previously Presented) The method of claim 1, wherein the amino acid sequence is at least 99% identical to amino acids 23 to 138 of SEQ ID NO:3.

32. (Previously presented) The method of claim 1, wherein the Fc portion is modified to reduce effector function.

33. (Previously presented) The method of claim 1, wherein the Fc portion is modified to reduce binding to an Fc receptor.

34. (Previously presented) The method of claim 1, wherein the Fc portion is modified to reduce complement activation.

35. (Previously presented) The method of claim 1, wherein the Fc portion is unmodified.

36. (Canceled)

37. (Canceled)

38. (Withdrawn-Currently Amended) The method of claim 1, wherein the ~~pharmaceutical composition is administered to a mammal in need of ameliorating a~~ symptom of disorder is muscle atrophy.

39. (Withdrawn-Currently Amended) The method of claim 1, wherein the ~~pharmaceutical composition is administered to a mammal in need of ameliorating a~~ symptom of disorder is muscle wasting syndrome.